Abstract: P5540

Familial clustering of spontaneous coronary artery dissection

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Topic(s):
Non-Atherosclerotic Coronary Abnormalities

Citation:
Background: There is increasing evidence that patients with spontaneous coronary artery dissection (SCAD) have an underlying genetic susceptibility (Goel et al JAMA Intern Med175:821-826, 2015). Moreover, in a collaborative study involving 1,055 SCAD cases and 7,190 controls, we recently reported the first risk allele for SCAD, a variant (rs9349379-A) in the PHACTR1/EDN1 genetic locus (Adlam et al J Amer Coll Cardiol73:58-66, 2019).

Purpose: We sought to determine the clinical characteristics and initial genetic data for 11 families, in which more than one member has had an episode of SCAD.

Methods: Participants were recruited largely via a social media platform. Informed consent was obtained in all cases for analysis of genetic information using whole genome sequencing, as well as collection of clinical information. SCAD was confirmed by review of coronary angiogram images and clinical data collected by phone interview, as well as review of specialist letters and hospital records.

Results: Of 235 participants recruited to date, 23 cases showed familial clustering involving sister-sister pairs in six families, three first-degree cousins in one family (picture), two first-degree cousins in two families, a mother-son pair, and a family with concordant monozygotic twins, that is both twins having had SCAD. In an additional family, SCAD is discordant in monozygotic twins. A comparison of symptoms, age at SCAD, clinical syndrome, cardiovascular risk factors, SCAD risk factors, environmental triggers, SCAD location, acute management, left ventricular function and recurrent SCAD events in these families versus isolated cases, will be presented. Three sister-sister pairs have undergone whole genome sequencing and these data sets are undergoing segregation analysis to identify rare variants that are present exclusively in affected family members.

Conclusions: To our knowledge, this is the largest assembly of SCAD cases with familial clustering reported to date. It provides strong evidence supporting an underlying genetic basis for SCAD, which most likely is a multi-genic disorder that also involves important gene-environment interactions.

Picture Legend: Shaded circles represent first cousins affected with SCAD. The top number represents age (in years) of the SCAD event and the bottom number represents current age (in years).
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